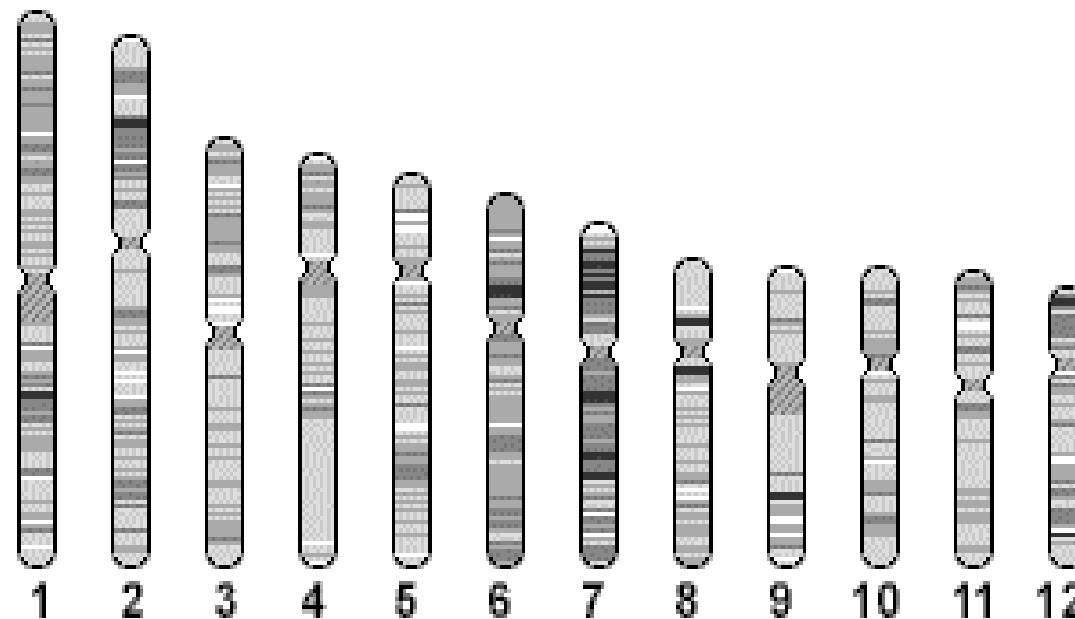
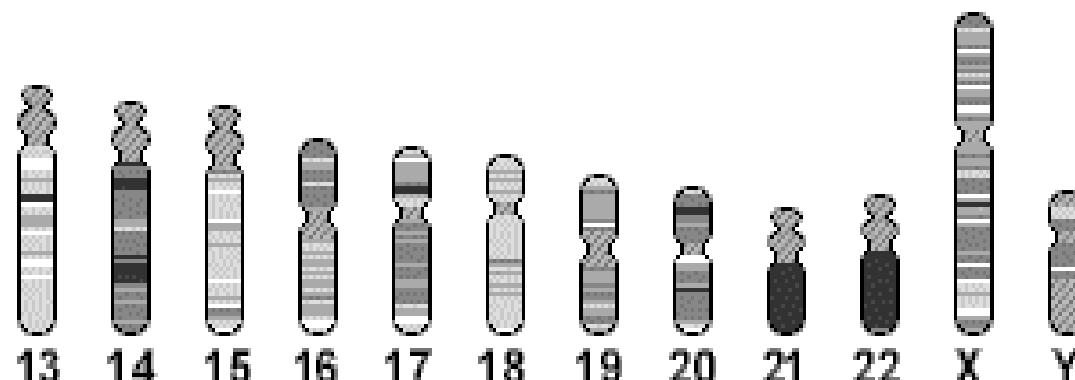


Human Sequencing: Current Progress



Sept. 18, 2000

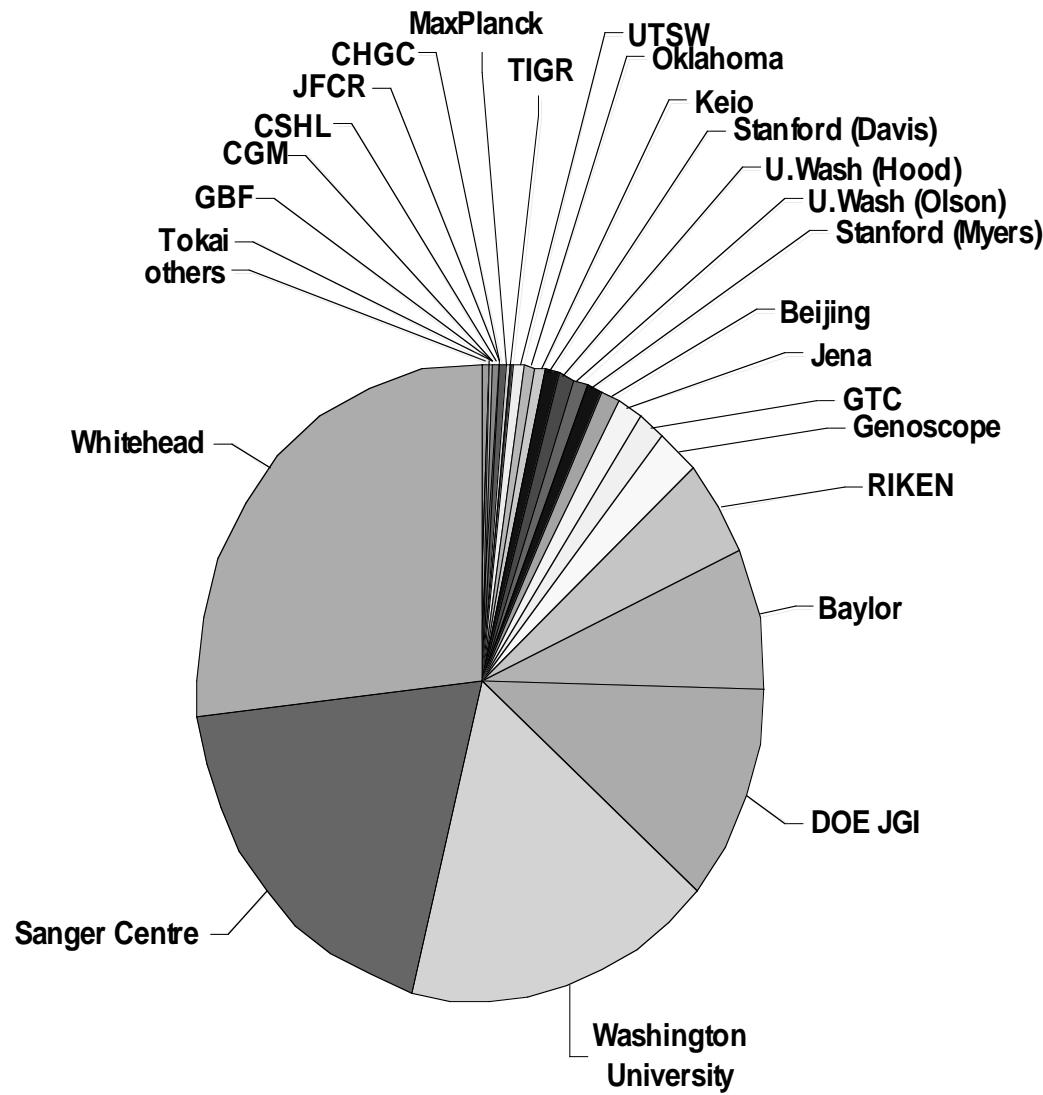
Draft: 66.2%
Finished: 24.7%
Total: 91.3%



■ > 1000 kb ■ 250 - 1000 kb ■ < 250 kb

□ draft sequence ■ heterochromatin

Human Genome Sequencing



2 December 1999

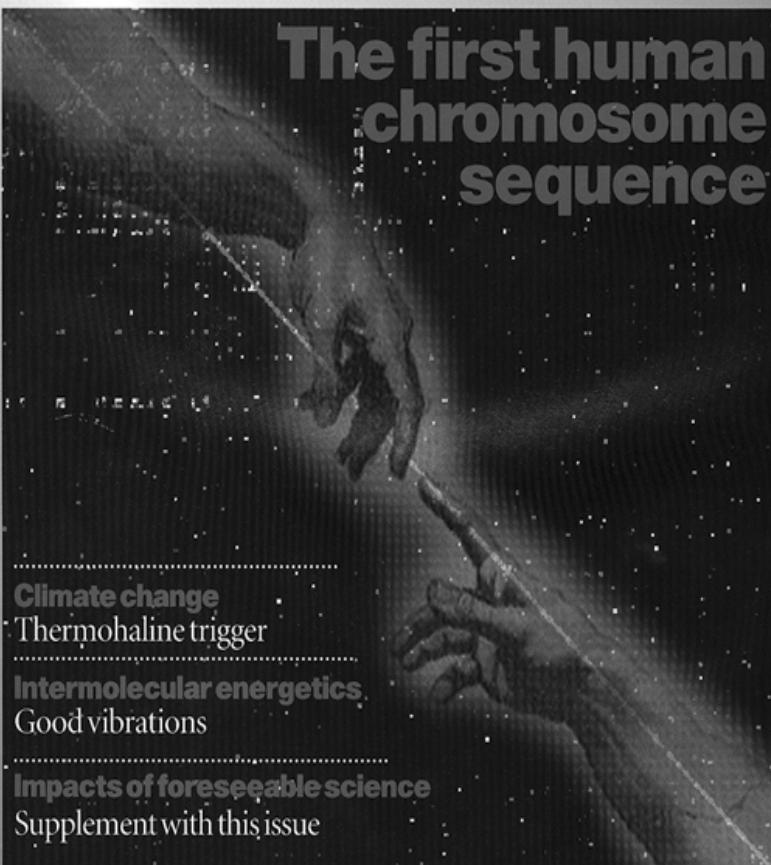
International weekly journal of science

nature

\$10.00

www.nature.com

The first human chromosome sequence



Climate change

Thermohaline trigger

Intermolecular energetics

Good vibrations

Impacts of foreseeable science

Supplement with this issue

New on the market

Lasers

The DNA sequence of human chromosome 22

I. Dunham, N. Shimizu, B. A. Roe, S. Chissoe *et al.*†

†A full list of authors appears at the end of this paper

Knowledge of the complete genomic DNA sequence of an organism allows a systematic approach to defining its genetic components. The genomic sequence provides access to the complete structures of all genes, including those without known function, their control elements, and, by inference, the proteins they encode, as well as all other biologically important sequences. Furthermore, the sequence is a rich and permanent source of information for the design of further biological studies of the organism and for the study of evolution through cross-species sequence comparison. The power of this approach has been amply demonstrated by the determination of the sequences of a number of microbial and model organisms. The next step is to obtain the complete sequence of the entire human genome. Here we report the sequence of the euchromatic part of human chromosome 22. The sequence obtained consists of 12 contiguous segments spanning 33.4 megabases, contains at least 545 genes and 134 pseudogenes, and provides the first view of the complex chromosomal landscapes that will be found in the rest of the genome.

***Nature* 402:489-495, 1999**

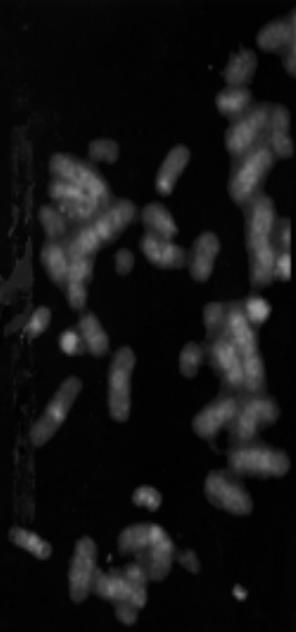
18 May 2000

International weekly journal of science

nature

\$16.00

www.nature.com



Counting down from 21

Optical microscopy A molecular light-bulb

Bioluminescence Jellyfish blues

Proglacial lakes Breaking their own dam

nature jobs focus

Postgraduate opportunities

The DNA sequence of human chromosome 21

The chromosome 21 mapping and sequencing consortium

M. Hattori^{†\$}, A. Fujiyama[†], T. D. Taylor[†], H. Watanabe[†], T. Yada[†], H.-S. Park[†], A. Toyoda[†], K. Ishii[†], Y. Totoki[†], D.-K. Choi[†], E. Soeda[†], M. Ohki[†], T. Takagi[†], Y. Sakaki^{†\$}, S. Taudien^{†\$}, K. Blechschmidt[†], A. Polley[†], U. Menzel[†], J. Delabar[†], K. Kumpf[†], R. Lehmann[†], D. Patterson[†], K. Reichwald[†], A. Rumpf[†], M. Schillhabel[†], A. Schudt[†], W. Zimmermann[†], A. Rosenthal[†]; J. Kudoh^{†\$}, K. Shibusawa[†], K. Kawasaki[†], S. Asakawa[†], A. Shintani[†], T. Sasaki[†], K. Nagamine[†], S. Mitsuyama[†], S. E. Antonarakis^{†\$}, S. Minoshima[†], N. Shimizu[†]; G. Nordsiek^{†\$}, I. Hornischer[†], P. Brandstetter[†], M. Scharfe[†], O. Schön[†], A. Desario^{†\$}, J. Reichelt[†], G. Kauer[†], H. Blöcker[†]; J. Ramsler^{†\$}, A. Beck^{†\$}, S. Klages^{†\$}, S. Hennig^{†\$}, L. Riessmann^{†\$}, E. Dagand^{†\$}, S. Wohrmeyer^{†\$}, K. Borzym^{†\$}, K. Gardiner[†], D. Nizet^{†\$}, F. Francis^{†\$}, H. Lehrach^{†\$}, R. Reinhardt^{†\$} & M.-L. Yaspo^{†\$}

Nature 405:311-319, 2000

Human Genome Sequence by the HGP

- Immediate Release**

Sequence Contigs >1-2 kb

Finished and Pre-Finished Sequence

- High Accuracy**

Error Rate of <1 in 10,000 bp

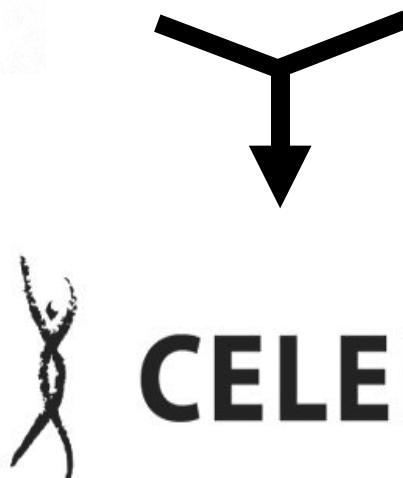
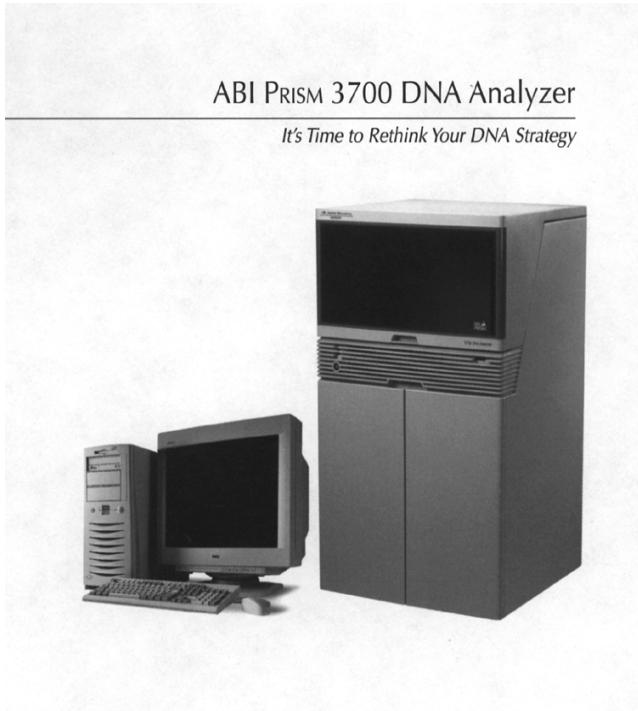
**Assessed/Confirmed by QC Exercises
(see *Genome Research* 9:1-4, 1999)**

- Cost**

**Steady (But Not Massive) Decrease
Currently at ~25-50¢ per Finished bp**

The Private Sector and DNA Sequencing

Commercial Interest in Human Genome Sequencing



CELERA



Whole-genome Shotgun Sequencing

Pros:

(Weber and Myers, 1997)

No sequence-ready maps required!
Savings of effort and cost

Much faster than clone-by-clone

Detection of DNA polymorphisms
Sequence 5 individuals

Cons:

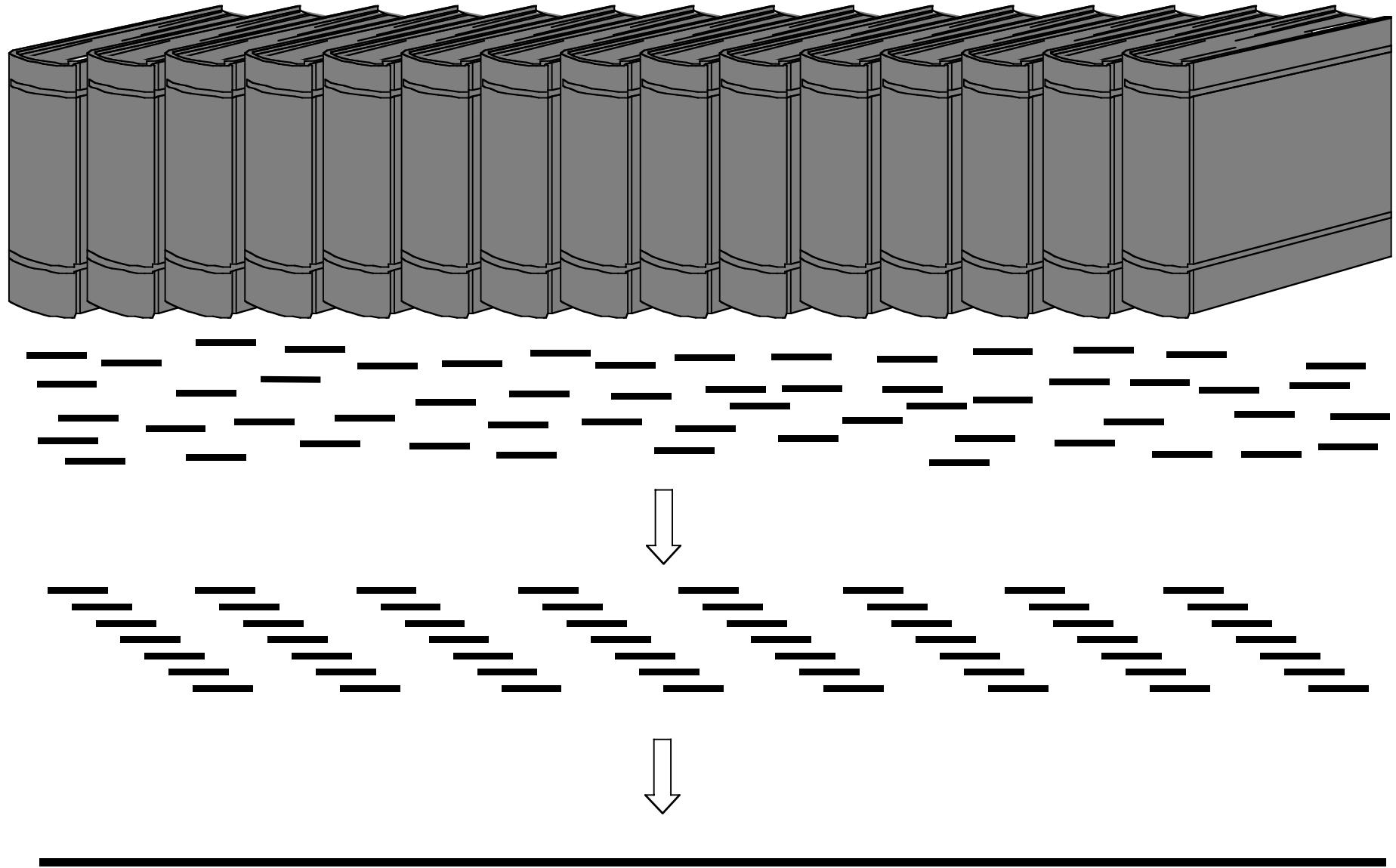
(Green, 1997)

Probability of success debatable

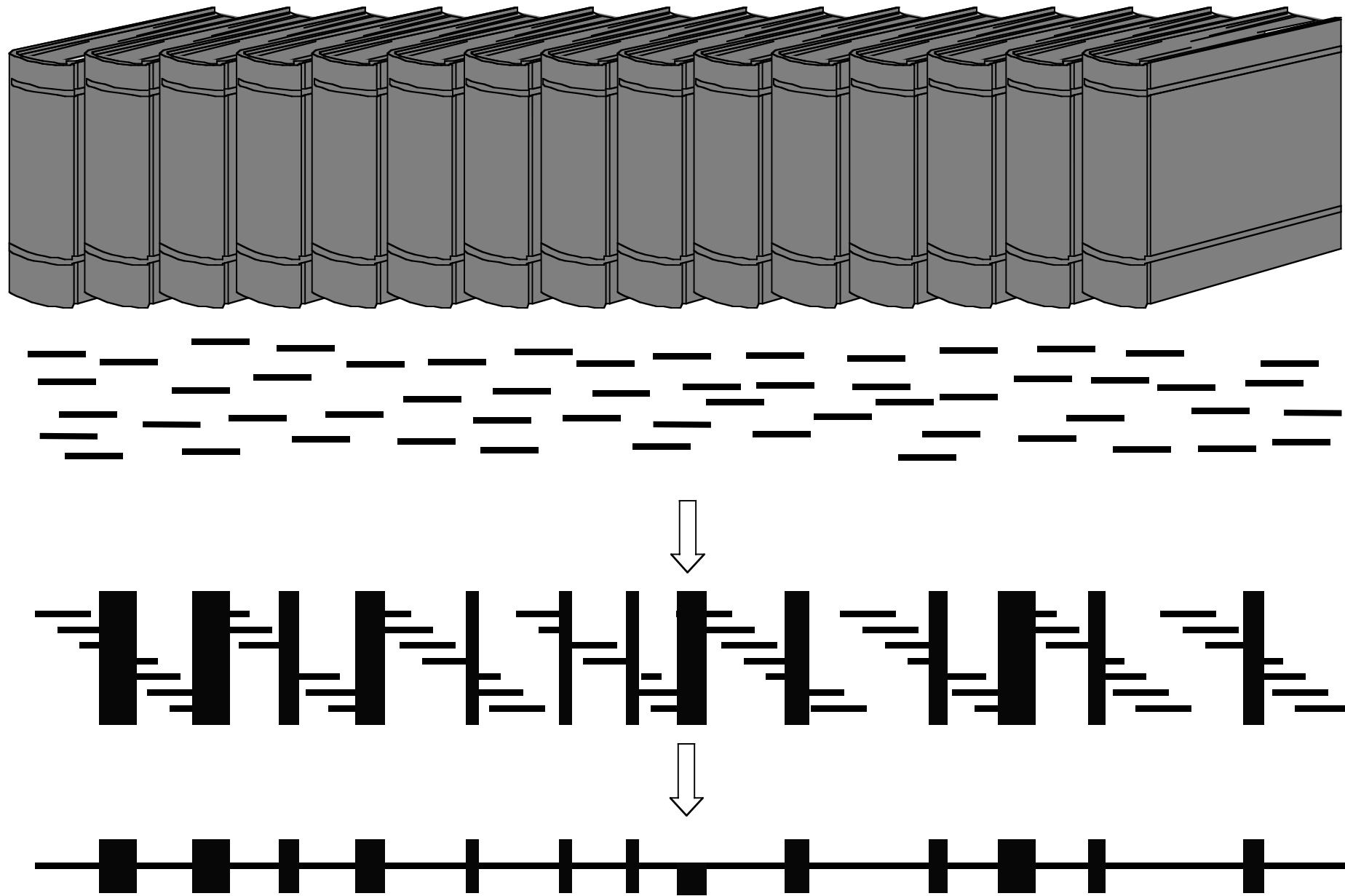
Cost savings ?
(“Finishing” could be a mess)

Final quality level ?

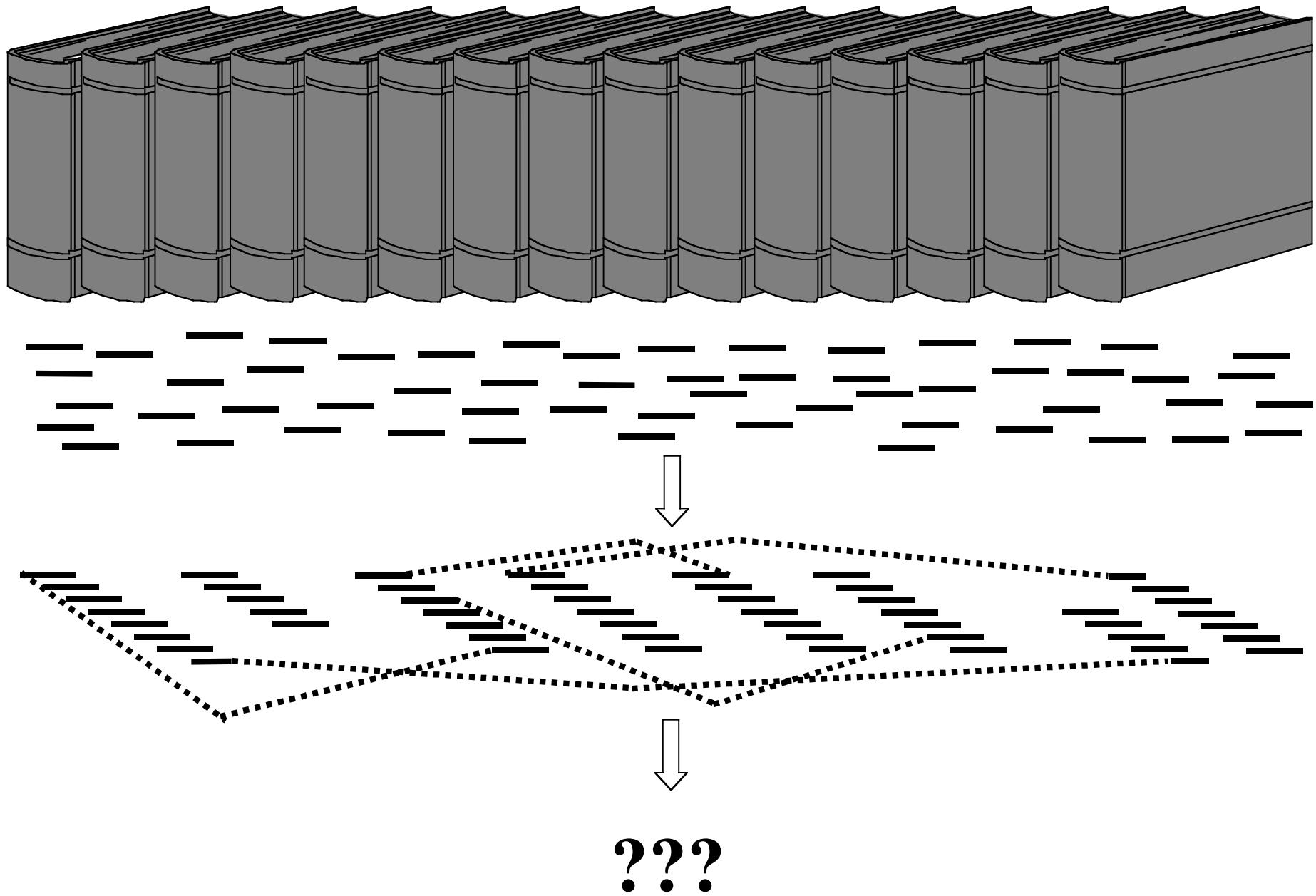
Whole Genome Shotgun Sequencing



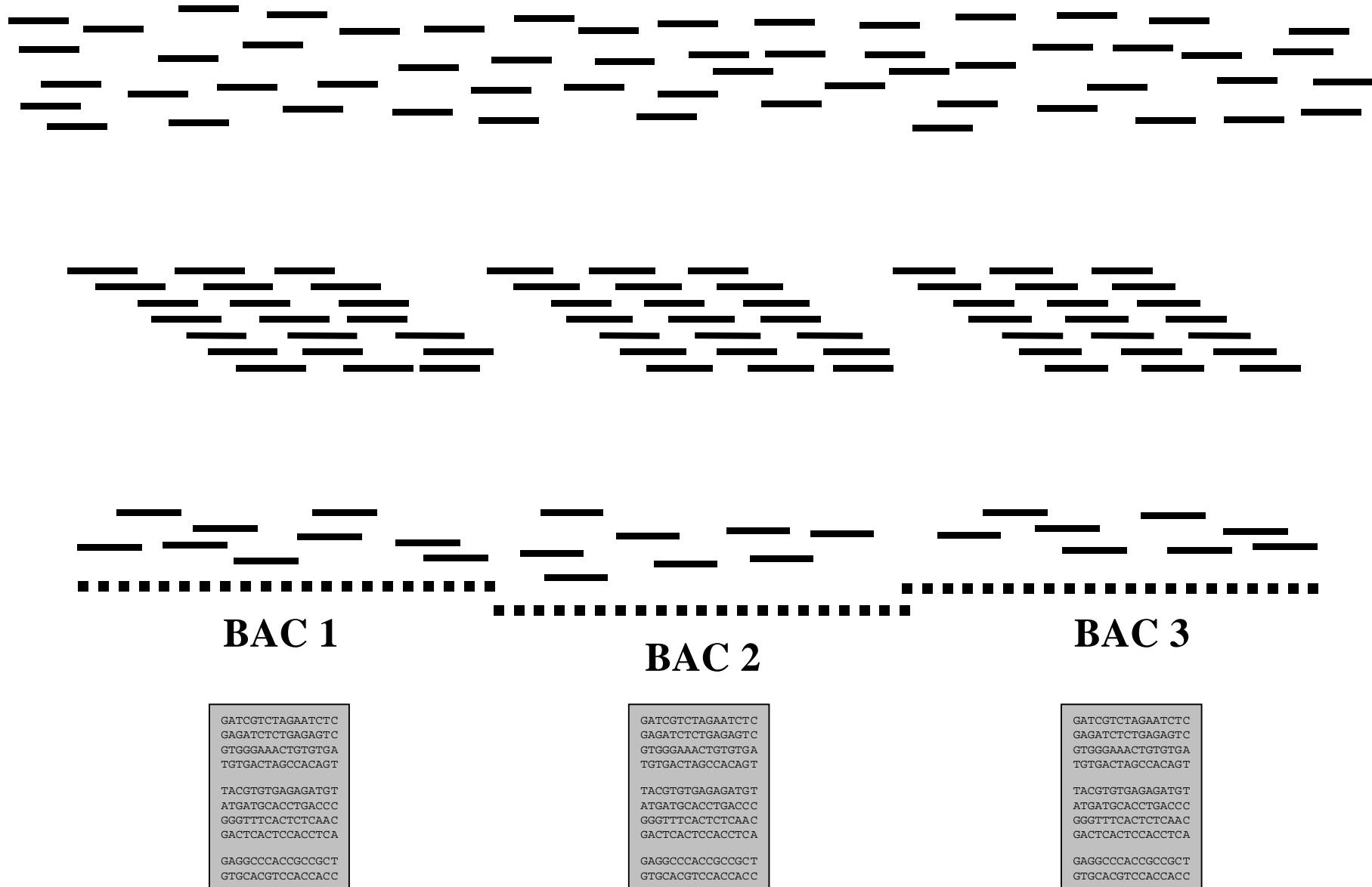
Whole Genome Shotgun Sequencing



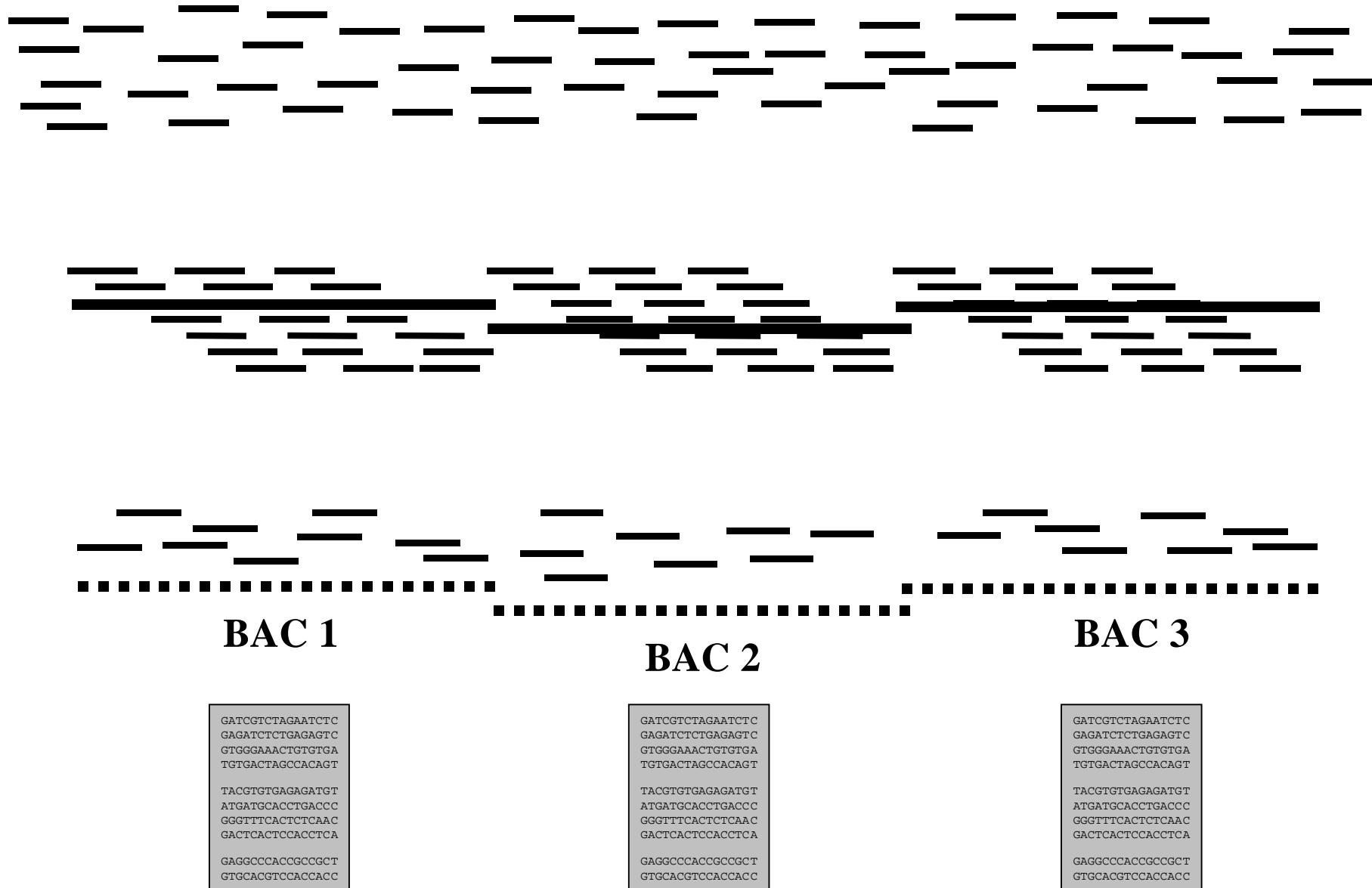
Whole Genome Shotgun Sequencing



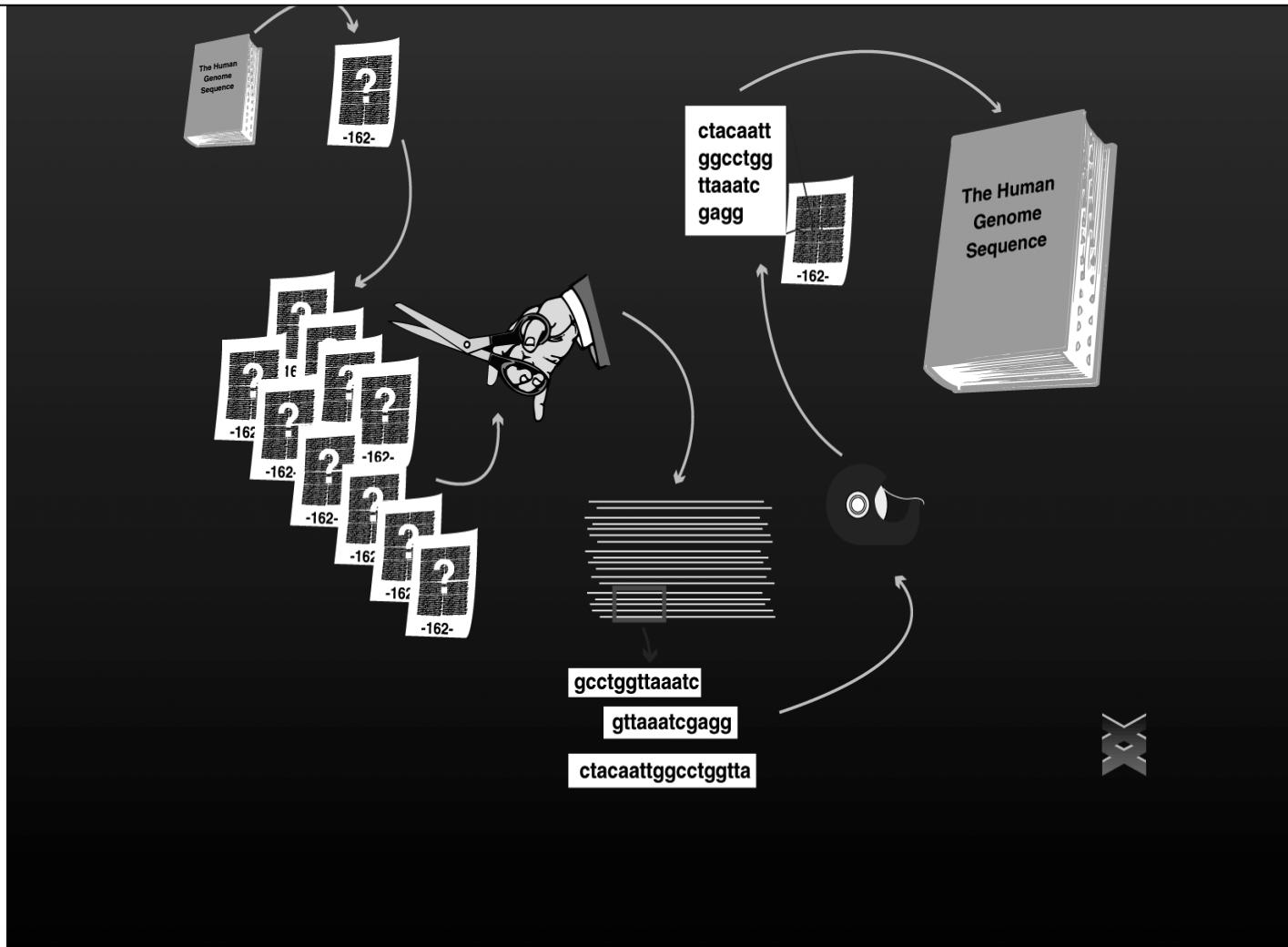
Hybrid Sequencing Strategy



Hybrid Sequencing Strategy

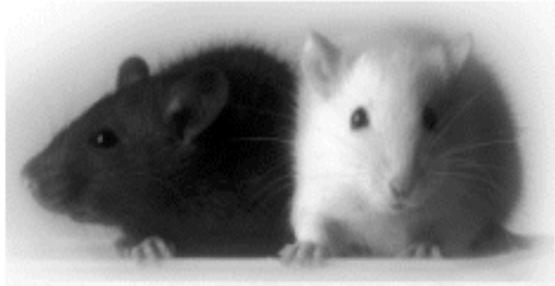


Sequencing Mapped DNA



Sequencing Other Genomes

Mouse Genome Analysis



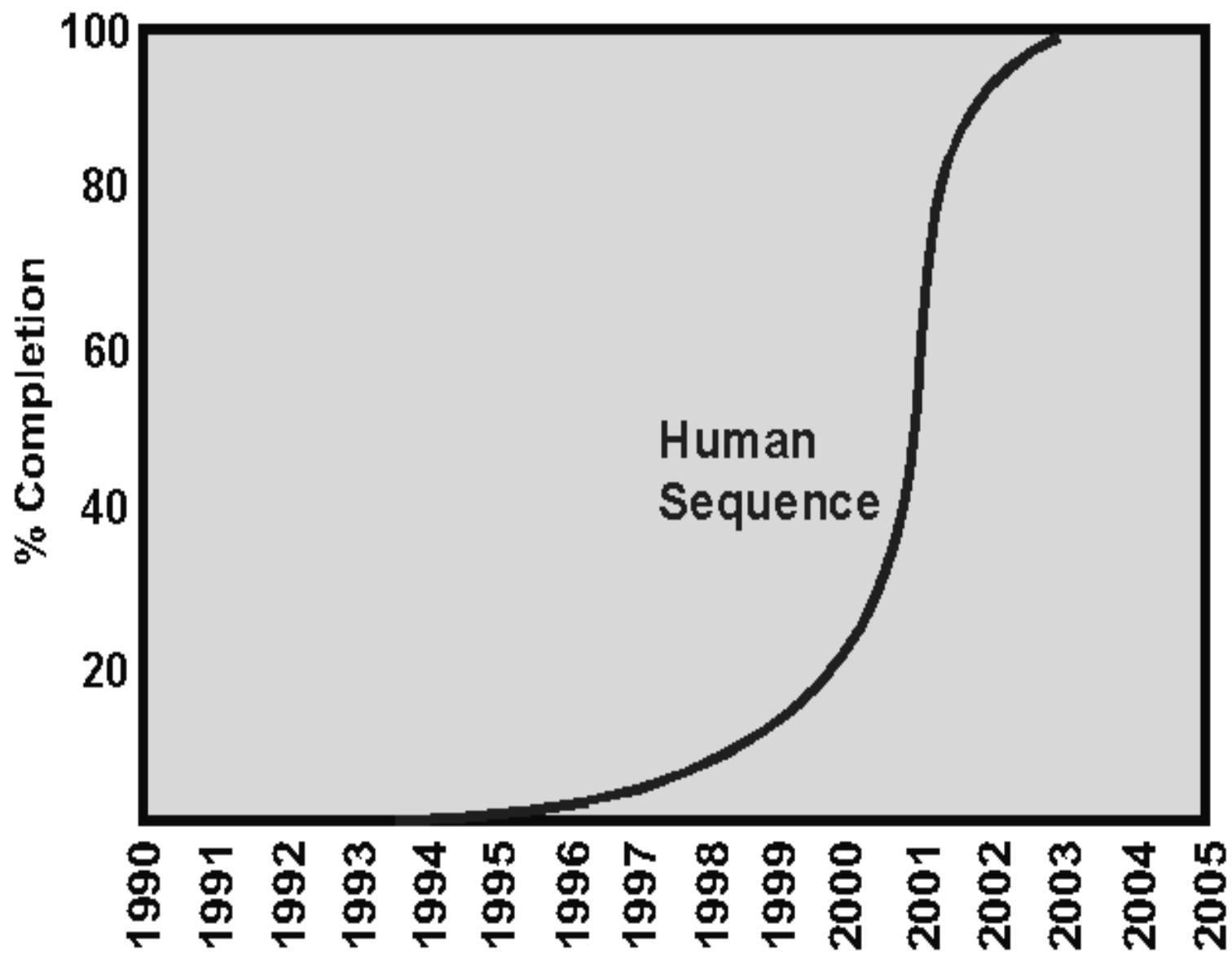
An action plan for mouse genomics

James Battey¹, Elke Jordan², David Cox³ & William Dove⁴

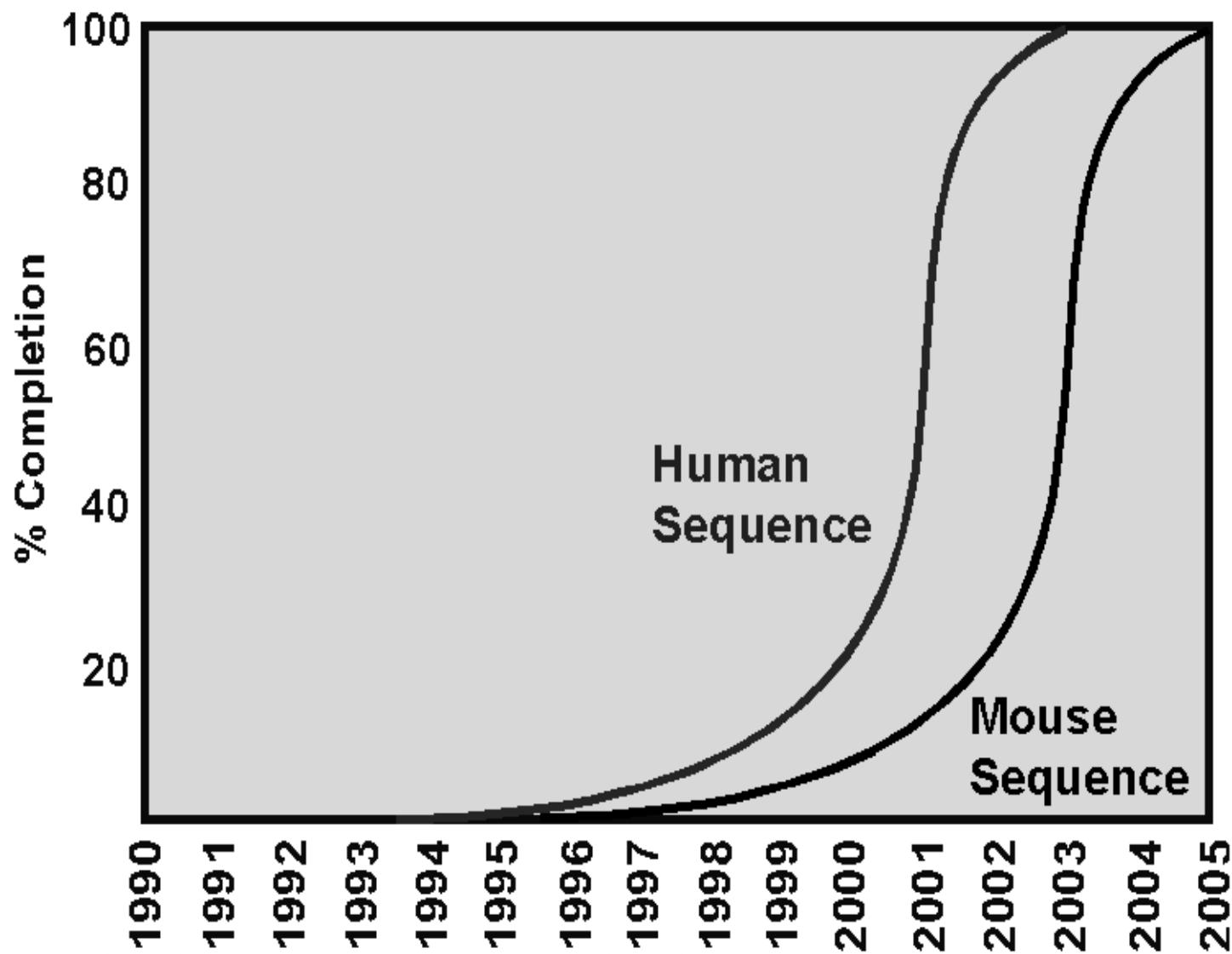
The mouse has become the leading animal model for studying biological processes in mammals. Creation of additional genomic and genetic resources will make the mouse an even more useful model for the research community. On the basis of recommendations from the scientific community, the National Institutes of Health (NIH) plans to support grants to generate a 'working draft' sequence of the mouse genome by 2003, systematic mutagenesis and phenotyping centres, repositories for mouse strain maintenance, distribution and cryopreservation and training fellowships in mouse pathobiology.

Nature Genetics 21:73-75, 1999
<http://www.nih.gov/science/mouse>

Highly Ambitious...



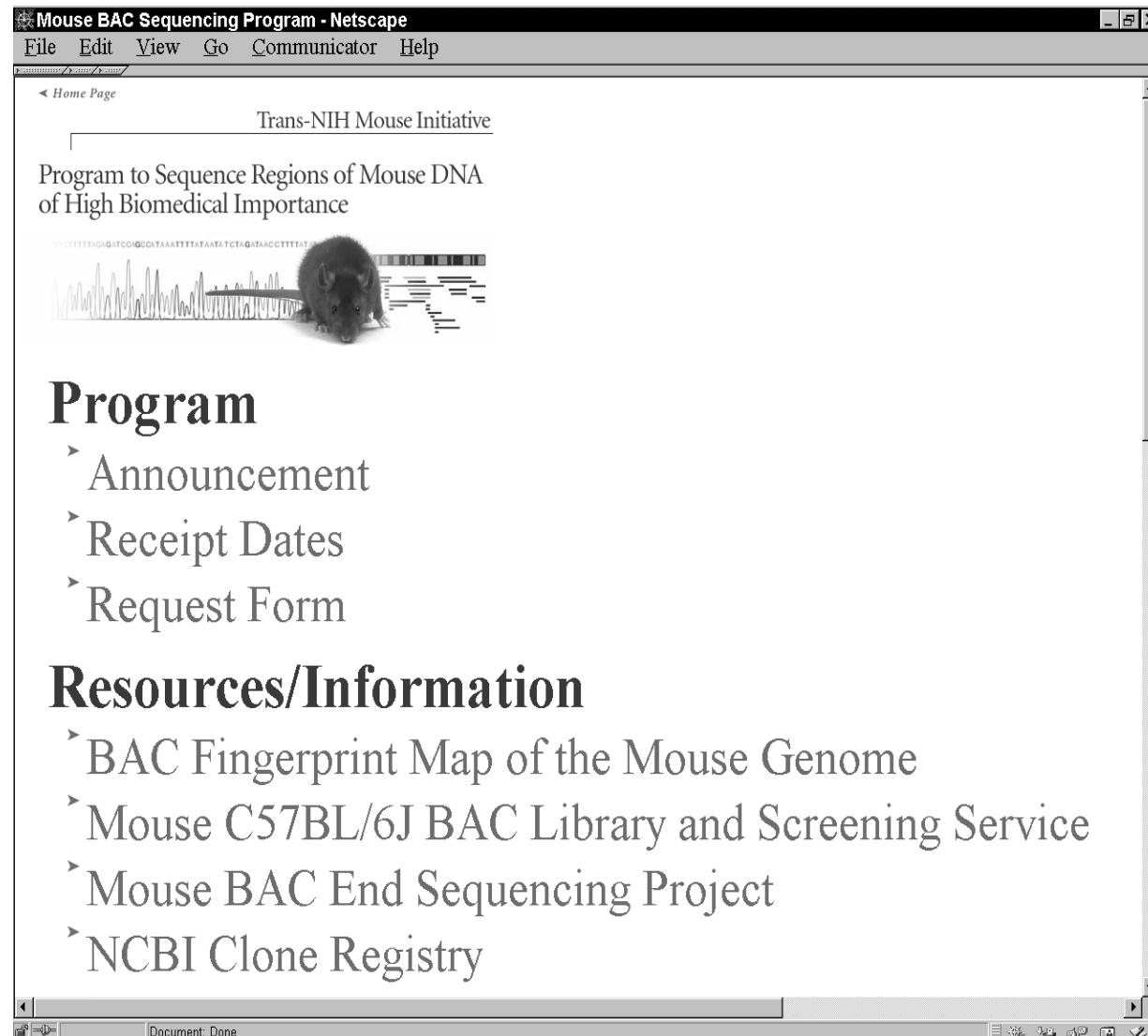
Even More Ambitious...



NIH Plan for Mouse Genome Sequencing

- **Consortium of Sequencing Centers**
 - Mapping Component: Fingerprints, End Sequences**
 - Sequencing Component: Global and Targeted Efforts**
- **Global Sequencing Efforts: “Hybrid Strategy”**
 - High Redundancy Whole-Genome-Shotgun Sequencing**
 - Low Redundancy BAC-by-BAC Sequencing**
- **Targeted Sequencing Efforts**
 - Prioritized Sequencing of Regions of Biomedical Importance**

Prioritized Sequencing of Regions of Biomedical Importance



<http://www.nih.gov/science/models/mouse/mouseseq>

Annotating the Human “Working Draft” with Mouse Sequence

progress

Shotgun sample sequence comparisons between mouse and human genomes

John B. Bouck, Michael L. Metzker & Richard A. Gibbs

Nature Genetics 25:31-33, 2000

Importance of Comparative Sequence Analysis

